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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,354	10/31/2001	Dennis M. Brown	A-70614/RFT/AMS	1942

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EXAMINER

DAVIS, RUTH A

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 06/26/2003

7.

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/996,354

Applicant(s)

BROWN, DENNIS M.

Examiner

Ruth A. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18 - 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 18 – 23 in Paper No. 6 is acknowledged.

Claims 1 – 17 and 24 have been cancelled; claims 18 – 23 are pending and have been considered on the merits.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 18 and 20 – 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Bombardelli et al. (US 5880160).

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member comprises a colchicine analog, specifically thiocolchicoside, 2-demethoxy-2-glucosidothiocolchicine.

Bombardelli teaches compositions comprising colchicine derivatives with antiproliferative activities (abstract). Specifically, wherein thiocolchicoside exhibits neoplastic (or antiproliferative) activity (col.1 line 18-29).

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The reference anticipates the claimed subject matter.

4. Claims 18 – 19 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Horrobin or Joseph.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide and the antiproliferation agent is vinblastine or paclitaxel.

Horrobin teaches a composition comprising colchicine and vinblastin (claim 10).

Joseph teaches compositions comprising paclitaxel and colchicine (abstract, claims 11-12).

The references anticipate the claimed subject matter.

5. Claims 18 – 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ratain.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide and the antiproliferative agent comprises etoposide, cisplatin or camptothecin.

Ratain teaches anticancer compositions comprising camptothecin and antineoplastic agents (col.8 line 65-67), to include colchicine (col.9 line 1-12).

The reference anticipates the claimed subject matter.

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6. Claims 18 – 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Fong.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent wherein the family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide.

Fong (1996) teaches synergistic compositions of colchicine and doxorubicin (antiproliferative agent) (abstract).

The reference anticipates the claimed subject matter.

7. Claims 18 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Belisario.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent wherein the family member comprises a colchicine analog.

Belisario (1965) teaches compositions of demecolcin (colchicine analog) and N-desacetyl thiocolchicine (antiproliferative agent) (abstract).

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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9. Claims 18 – 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bombardelli.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide; a colchicine analog; or thiocolchicoside, 2-demethoxy-2-glucosidothiocolchicine.

Bombardelli teaches compositions comprising colchicine derivatives with antiproliferative activities (abstract). Specifically, wherein thiocolchicoside exhibits neoplastic (or antiproliferative) activity (col.1 line 18-29).

Bombardelli does not teach the composition comprising colchicine. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to substitute colchicine in place of its derivative since it was well known in the art that analogs commonly exhibit the same activity. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to substitute colchicine in the composition of Bombardelli with a reasonable expectation for successfully obtaining an antiproliferative composition.

10. Claims 18 – 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horrobin or Joseph.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-

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tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide; a colchicine analog; or thiocolchicoside, 2-demethoxy-2-glucosidothiocolchicine and the antiproliferation agent is vinblastine or paclitaxel.

Horrobin teaches a composition comprising colchicine and vinblastin (claim 10).

Joseph teaches compositions comprising paclitaxel and colchicine (abstract, claims 11-12).

The references do not teach the compositions comprising the claimed colchicine analogs. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to substitute colchicine analogs in place of colchicine since it was well known in the art that analog compounds commonly exhibit the same activity. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to substitute colchicine with it's analogs with a reasonable expectation for successfully obtaining either of the disclosed compositions.

11. Claims 18 – 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frisch, Houghton, and/or Ratain.

Applicant claims a composition comprising a colchicine family member and an antiproliferative agent. The family member is colchicine, (S)-N—(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl) acetamide; a colchicine analog; or thiocolchicoside, 2-demethoxy-2-glucosidothiocolchicine. The antiproliferative agent comprises etoposide, cisplatin or camptothecin; or alternatively vinblastine or paclitaxel.

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Frisch teaches compositions comprising chemotherapeutic agents selected from etoposide, camptothecin, colchicine, cisplatin and vinblastine (claims).

Houghton teaches anticancer (antiproliferative) compositions comprising a cytotoxic (or antiproliferative) agent and a potentiating agent (claim 29). Cytotoxic agents include vinblastine, etoposide, colchicine and mixtures thereof (claim 29-30).

Ratain teaches anticancer compositions comprising camptothecin and antineoplastic agents (col.8 line 65-67), to include colchicine (col.9 line 1-12). Ratain teaches that camptothecin (col.14) vinblastine, colchicine, etoposide and analogues thereof are antineoplastic, or antiproliferative (col.9 line 1-12).

The references do not teach each composition comprising the claimed combinations of components. However, each of the cited references teach the individual components are effective antiproliferative agents. At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for their claimed purpose. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Moreover, at the time of the claimed invention one of ordinary skill in the art would have been motivated by the cited references, alone or in combination, to combine the instant ingredients with a reasonable expectation for successfully obtaining an effective antiproliferative composition.

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Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 18 – 23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 – 13 of copending Application No. 09/810,527. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to combine known antiproliferative agents and their analogs into a single effective antiproliferative composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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14. Claims 18 – 23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 – 13 of copending Application No. 09/834,177. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to combine known antiproliferative agents and their analogs into a single effective antiproliferative composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted that application 09/834,177 has been issued a notice of allowance on May 1, 2003.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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Ruth A. Davis; rad
June 23, 2003



LEON B. LANKFORD, JR.
PRIMARY EXAMINER